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The effects of vildagliptin in liver functions in type 2 diabetic patients

Effect of vildagliptin on liver function

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Abstract

Aim: In Type 2 diabetic patients, the prevalence of liver disease is high when compared with the general population. For this reason, the hepatic safety of anti-diabetes agent is important. However, there are uncertainties about the long-term efficiency and reliability of vildagliptin treatment. In this study, we have reviewed the findings obtained from the clinical use of vildagliptin and its effects on the liver. Material and Method: The study was conducted on 243 patients who were followed-up in our clinic between September 2016 and May 2018. The data were obtained by reviewing the patient files retrospectively. Result: A decrease was detected in the aminotransferases after the treatment with vildagliptin, which was statistically significant (ALT: decreased from 78 ± 17 to 48 ± 14 IU / L (p = 0.029), AST: decreased from 63 ± 13 to 41 ± 11 IU / L (p=0.035); GGT: 20.5±3.2 and 19.1±6.3 (p=0.682)). Vildagliptin reduces the insulin resistance and Body Mass Index in patients. Discussion: It was determined that Vildagliptin is a safe treatment option for Type 2 Diabetes management.

Keywords

Type 2 Diabetes; Vildagliptin; Safety; Liver Functions

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Introduction

Vildagliptin is a dipeptidyl peptidase-4 (DPP-4) inhibitor for the treatment of Type 2 Diabetes Mellitus (T2DM). Since DPP-4 inhibitors provide glucose control with a low hypoglycemia risk, they attract attention among therapeutic treatment options for T2DM [1]. Twice-daily application of vildagliptin is recommended because of its shorter half-life, and most of the other DPP-4 inhibitors allow oral application once a day for T2DM management. While vildagliptin is mostly metabolized before it is removed, most of the other DPP-4 inhibitors are removed with the urine without joining the metabolism. This allows the use of Vildagliptin in patients who have kidney failure [2]. In patients with T2DM, the prevalence of liver disease is high when compared with the general population. For this reason, it is important to ensure the hepatic safety of anti-Diabetes agent. The proof obtained in toxicology studies and in in-vitro studies did not indicate hepatotoxicity risk [3]. However, there are uncertainties about the long-term use and reliability of vildagliptin treatment [4]. In this manuscript, the files of the patients who used this medicine were reviewed and the findings obtained from the clinical use of vildagliptin were used to review its effects on the liver.

Material and Method

This is a retrospective observational study conducted to evaluate the reliability of vildagliptin on the liver in order to ensure glycemic control in diabetes management in Type 2 diabetes patients who received vildagliptin. The file of each patient was reviewed retrospectively and the clinical laboratory tests (mainly the blood and biochemical tests) at the beginning of the vildagliptin treatment; and the clinical laboratory test values of the individuals who visited the clinic regularly for the 3-6th months were recorded.

The study was conducted on the patients who were followed-up in our clinic between September 2016 and May 2018. The patients who met all of the following criteria were included in the study: New diagnosis of Type 2 Diabetes, 6-month diet and exercise therapy and blood sugar not controlled, having spent ≥6 months since the beginning of the metformin plus vildagliptin or only vildagliptin treatment. Any of the patients who met the following criteria were excluded from the study: Type 1 diabetes, acute hepatic dysfunction, cardiovascular disease in the past 6 months, malignant tumor and using medication that might increase the liver enzymes.

Statistical Analysis

The analysis of the data was made in theSPSS version 10.0 [SPSS Inc, Chicago, IL] program. The descriptive analysis was made by using mean ± standard deviation (SD), and the one-way ANOVA analysis was used in comparing the groups. Among the groups, the Kruskal-Wallis Test was used for further analyses. The categoricalvariables were evaluated with the Pearson Chi-Square Test. Paired t-test and intergroups t-test or the Mann-Whitney U-test were used in each group. The statistical data were considered significant if P<0.05.

Results

A total of 234 cases (100 male, 143 female) were included in the study. The mean age of the patients was 45.39 ± 14.72 years. The body weight decreased to 84 ± 9 kg from 92 ± 12 kg with the vildagliptin treatment. The Body Mass Index (BMI) decreased to 27.5 ± 13 from 31.2 ± 3 (p=0.027). The basal properties of the cases are given in Table 1. The HbA1c values decreased to 6.8 ± 0.6% (p=0.016) from 9.6 ± 0.7% with the vildagliptin treatment. Meanwhile, there was a clear decrease in the initial values of the TC, TG, and LDL-C, and a statistically significant increase was determined in the HDL-C value. After the treatment with vildagliptin, a clear decrease was determined in the aminotransferase level; ALT: decreased from 78 ± 17 to 48 ± 14 IU / L (p = 0.029), AST: decreased from 63 ± 13 to 41 ± 11 IU / L (p=0.035), and the GGT: 20.5 ± 3.2 and 19.1 ± 6.3 (p=0.682). It was observed that the vildagliptin decreased the insulin resistance in the patients, HOMA-IR: decreased from 6.5 ± 2.7 to 3.2 ± 1.3 μ U/mol/L (p=0.002). The changes in the parameters before and after the treatment with vildagliptin are given in Table 2. Minor hypoglycemia was reported in two patients with vildagliptin. No findings like pancreatic, arthralgia, upper respiratory tract infections were reported depending on the medication.

Table 1. Baseline characteristics of study groups

Baseline Characteristics	Vildagliptin pre- treatment (n: 243)	Vildagliptin post-treatment (n: 243)
Age (years)	45.39±14.72	45.39±14.72
Sex Male / Female	100/143	100/143
BMI, kg/m^2	30.7±4.2	27.5±5.2
Duration of disease (month)	3.8±2.6	8.3±3.1

Values are given as mean ± standard deviation, BMI: Body Mass Index

Table 2. Results of vildagliptin pre and post treatment

Parameters	Vildagliptin Pre- treatment	(n : 243) Post-treatment	P value
BMI , kg/m^2	30.7±4.2	27.5±5.2	0.027
Blood sugar fasting, mg/dl	195±27	125±18	0.004
Hba1c ,%	% 9.6 ± 0.7	% 6.8 ± 0.6	0.016
TC, mg/dl	242.6±23.1	194±17.5	0.031
HOMA-IR, μU/mol/L	6.5±2.7	3.2±1.3	0.002
LDL-C, mg/dl	172±12.5	135±11.2	0.004
HDL-C, mg/dl	28.6±6.7	42.4±6.3	0.042
ALT, IU/L	79.2±18.9	43.4±15.1	0.029
AST, IU/L	64.2±9.8	39.5± 8.9	0.035
GGT, IU/L	20.5±3.2	19.1±6.3	0.682
Creatinine, mg/dL	0.87±2.7	0.76±1.5	0.743

Results are expressed as mean ± standard deviation.
BMI: body mass index, Hba1c: glycosylated hemoglobin type a1c, TC: Total Cholesterol, HOMA-IR: homeostasis model assessment of insulin resistance, LDL-C: low density lipoprotein cholesterol, HDL-C: high density lipoprotein cholesterol, ALT: alanine aminotransferases, AST: aspartate aminotransferases, GGT: gamma glutamyl transpeptidase.

Discussion

In our study, we determined that with the vildagliptin treatment, Type-2 Diabetes was managed well, the treatment was well-tolerated, hypoglycemia incidence was low, fasting blood sugar and Hba1c decreased in an efficient manner, and it had a good general safety profile. In addition, we showed the efficiency of

vildagliptin and metformin combination on the Hba1c reduction and the reduction effects of these on body weight. With the use of these, the reduction in the Hba1c and rare hypoglycemia and weight loss and incretin hormonesmight contribute to these effects. In addition to the blood sugar control, vildagliptin has a potential role in the non-alcoholic liver fattening treatment. The insulin resistance is an important metabolic abnormality for these patients and this serum reduces the DPP-4 activity because hepatic fattening is associated with increased DPP-4 in these patients. The portal inflammation decreases as a result of the decrease in the DPP-4 level [5,6]. In our study, the liver amino transferase enzymes decreased and were statistically significant. It is possible to claim that Metformin and vildagliptin combination reduced the insulin resistance and DDP-4 activity, which contribute to this situation. Vildagliptin inhibits the dipeptidylpeptidase-IV (DPP-4) enzyme and increases the glucagon-like peptide 1 (GLP-1) and glycose-dependent insulinotropic polypeptide (GIP) physiological concentration in the body. It also inhibits the glucagon secretion, which causes insulin release, and reduces the hypoglycemia risk and the risk of weight gain at a further level by increasing the GLP-1 level, which delays the gastric evacuation and reduces the appetite [7]. We showed that our patients lost weight and their BMI decreased at a significant level. The loss of weight contributes to the normalization of the liver enzymes. In addition, mild hypoglycemia was reported in 2 of our patients. In previous studies, it has been shown that vildagliptin, which is a dipeptidyl-peptidase-4 inhibitor, decreased hepatic glyceride levels at a clinically significant level during 6-month treatment period independently from the changes in the body weight [8,9]. For the first time, it was shown that DPP-4 inhibition might cause clinically beneficial decreases in the liver triglyceride levels which is associated with a decrease in plasma ALT and plasma glucose. In our study, we determined decreases in the triglycerideand LDL-C levels. The decrease of the triglyceride in the liver regresses the hepaticsteatosis andcontributes to the normalization of the liver enzymes. Vildagliptin risk profile has not changed at a significant level in recent years. This product is used commonly in clinical settings and rare side effects as pancreatitis, hepatitis, bullous or exfoliative skin lesions and arthralgia were reported only in a few studies [10]. Vildagliptin continues to be an important treatment option to manage T2DM patientswith thehelp of its established safety profile [11,12]. In our study, no cases were detected reporting such side effects. This study had a number of limitations due to its retrospective observational design. Data from an unselected group of the patients was used and the size of the patient population was not as large as in other studies conducted in patients with type 2 diabetes. In our study, other studies and systemic reviews and meta-analyses were examined.

Conclusion

It was determined that vildagliptin is a safe treatment option for T2DM patients both as a monotherapy and as an additional treatment. No contraindications were reported for specific populations (the elderly, or patients with kidney failure) aside from excessive sensitivity to the active substance it contains and it is also used for this population [12]. The proof obtained in the our study made us consider that vildagliptin is safe in managing type 2 diabetes because it is consistent with the world data which includes a wide population.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

None of the authors received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.

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